

REMARKS

Claims 22 and 24-32 are pending in this application for the Examiner's review and consideration. Applicants are awaiting a certified copy of the priority document, Mexican Application Number 998515, as required by 35 U.S.C. § 119(b) and will submit the certified copy as required by the Examiner in a supplemental amendment as soon as it is received. Claims 22 and 28-32 have been amended to more clearly recite the claimed embodiments. Claim 23 has been canceled and its subject matter has been incorporated into claim 22. No new matter has been added by the amendments.

I. The Rejections Under 35 U.S.C. § 112, Second Paragraph

Claim 22 is rejected on pages 2-3 of the Office Action under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter, which applicant regards as the invention.

According to the office action, it is unclear as to the metes and bounds of what would be considered "unitary doses." The Office Action alleges that "it is still unclear how many viral particles is considered a 'unitary dose.'"

Applicants respectfully submit that they have amended claim 22 to recite that the unitary dose comprises from about 10^7 - 10^{14} viral particles. Applicants respectfully submit that in view of the amendment, the rejection of claim 22 under 35 U.S.C. § 112, second paragraph, should be reconsidered and withdrawn.

Claims 22, 23, and 28-32 are rejected on pages 3-4 of the office action under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter, which applicant regards as the invention.

According to the office action, the phrase "the therapeutic for the treatment of fibrotic disorders the latent and/or active protein MMP-8, MMP-1, MMP-2, MMP-9, MMP-3, uPa wild type and/or modified; the truncated receptor for TGF-beta type II; betaglycan; HGF; and Smad-7"

in claim 22 is vague and renders the claim indefinite. Applicants have amended claim 22 thus rendering the rejection moot.

The Office Action further alleges, the terms “MMP,” “uPa,” “TGF,” and “HGF,” in claim 22 are vague and render the claim indefinite. Applicants have amended the claim to spell out each of these terms. Applicants respectfully submit that “Smad 7” is not an abbreviation and one of ordinary skill in the art would understand what is meant by this term.

According to the Office Action, the term “and/or” in lines 7 and 8 of claim 22 is vague and renders the claim indefinite. Applicants respectfully submit that they have amended claim 22 thus rendering the rejection moot.

According to the office action, claim 28 recites the limitation “the administration route is intravenous” in lines 1-2. The Office Action alleges that there is insufficient antecedent basis for this limitation in the claim. Applicants respectfully submit that they have amended claim 28 thus rendering the rejection moot.

II. Claim Objections

Claims 28-32 are objected to under 37 C.F.R. § 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicants respectfully submit that they have amended claims 28-32 thus rendering the rejection moot.

III. The Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 22-27 are rejected on pages 4-10 of the office action under 35 U.S.C. § 112, first paragraph. According to the office action, the claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Office Action further alleges that the specification fails to provide adequate guidance and evidence for delivering a recombinant adenoviral vector expressing any therapeutic protein under the control of a promoter via various administration routes *in vivo* such that therapeutic effects can be obtained so as to treat any fibrotic disease or disorder in a patient.

As the Examiner is aware, the test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosure in the patent coupled with information known in the art without undue experimentation. *United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988), cert. denied, 490 U.S. 1046 (1989). The policy served by the test is to ensure that, in return for the grant of exclusivity provided by a patent, the inventor has provided a disclosure which enables the public to make and use his invention after the expiration of the patent. *Grant v. Raymond*, 31 U.S. 218, 247 (1832). A patent need not disclose what is well known in the art. *In re Wands*, 858 F.2d at 735. Not every last detail is to be described, else patent specifications would turn into production specifications, which they were never intended to be. *In re Gay*, 309 F.2d at 774. Thus, omissions in the specification do not render a patent invalid under the enablement standard, unless the omissions cause one skilled in the art to perform undue experimentation in order to practice the invention. *Hormone Research Foundation v. Genentech, Inc.*, 708 F. Supp. 1096, 1107 (N.D. Cal. 1988), *aff'd in part, vacated in part, and remanded*, 904 F.2d 1558 (Fed. Cir. 1990).

Importantly and the Applicants stress, “the enablement requirement is met if the description enables any mode of making and using the claimed invention” and not every mode. *Engel Industries, Inc. v. Lockformer Co.*, 946 F.2d 1528 (Fed. Cir. 1991). Enablement “is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive.” *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1987).

The Office Action alleges, “[c]laims 22, 23, and 28-32 encompass treating various diseases or disorders in a patient by delivering a recombinant adenoviral vector expressing the recited therapeutic protein under the control of a promoter via various administration routes *in vivo*.” First, although the Examiner is correct that the compositions can be used to treat diseases and disorders in a patient, Applicants point out that claims 22 and 28-32 are composition claims and not method of treatment claims.

With regard to claims 22 and 28-32, Applicants respectfully traverse the rejection. Applicants respectfully submit that the specification as-filed provides an enabling disclosure of representative embodiments of the claimed composition, as required under 35 U.S.C. § 112, first

paragraph, and confirmed by the Federal Circuit in *Engel Industries, Inc.* In particular, the specification as-filed discloses:

The current invention initiates a research line to carry out gene therapy as an alternative for the treatment of chronic degenerative disease, specifically of hepatic cirrhosis in human beings, through the establishment of an efficient vehicle to send genes to the liver which will produce therapeutic proteins to help re-establish the normal functions of the liver, see FIG. 2. FIG. 2 shows how sending efficiently a therapeutic gene to the liver, in this case, a collagenase (metalloproteases of matrix, MMPs), it is possible to promote degradation of collagen through the over-expression of these metalloproteases.

(See Specification of published application at Par. [0065]).

In FIG. 3, the strategy for the cloning and production of an adenoviral vector is shown. The plasmid pDeltaE1sp1B contains adenovirus Ad5 sequences, in which the bacterial gene Lac-z was inserted. This plasmid was recombined with the pBHG10 to obtain complete viral particles after co-transfection in the cell line 293. The vector pAdGFP was obtained as follows: the MMP-8 gene (coming from the plasmid PEPCK-MMP-8) was cloned in the vehicle vector, pAdTrack-CMV, the resultant plasmid is linearized with the restriction endonuclease Pme I, and is then transformed in *E. coli* (BJ5183) with the plasmid pAdEASY-1. The recombinant colonies were selected through kanamycin resistance, and the recombination is confirmed by restriction analysis with endonucleases. Finally, the recombinant plasmid linearized is transfected in the packaging cell line (293 cells), the recombinant adenoviruses are obtained within 7 to 12 days as illustrated in FIGS. 3 and 4 (Tong Chuan H., Shibin Z., Luis T. Jian Y, Kenneth W. and Volgestein Bert: A simplified system for generating recombinant adenoviruses. *Prod. Natl. Acad. Sci. USA* Vol. 95: 2509-2514, March 1998). To evaluate the grade of transduction in vitro liver HepG2 cell line and peritoneal macrophages isolated from mouse were used. In FIG. 5 the expression of -galactosidase in cultured cells is shown. A), B) and C) correspond to HepG2 cells (320.times.); D), E) and F), are mouse peritoneal macrophages (100.times.). In C) and F) the transduced cells are shown with 1.times.10.sup.8 viral particles/ml from the Ad5-Gal vector. Three techniques were conducted to compare the degree of incorporation of the reporter gene Lac-Z which was administered to each culture

dish in the form of plasmidic DNA PGK-Gal, through precipitation with Ca^{++} phosphate (Chen C, and Okayama H. Calcium Phosphate mediated gene transfer, a highly efficient system to establish transforming cells with plasmidic DNA. *Biotechniques* 1988, 6:632-638), DNA complexes-polylysine-Lactose (Martinez-Fong D., Mullersman J E, Purchio A F, Armendariz-Borunda J., and Martinez-Hernandez A., Non enzymatic glycosylation of poly-L-lysine: A new tool for targeted gene delivery. *Hepatology*, Vol. 20, No. 6: 1602-1608), with the vectors -Ad5-gal and pAdGFP-MMP8. The visualization of the activity of Gal was verified with the reactive Xgal and the GFP in a microscope-stereoscope of fluorescence. For the in vivo assay, gal staining was standardized using different pHs of the suspension with the reactive Xgal (Weiss D J, Ligitt D., and Clark J G. In situ photochemical detection of galactosidase activity in lung: assessment of Xgal reagent in distinguished Lac-Z gene expression and endogenous galactosidase activity. *Human being therapy*, Sep. 1, 1997, 8:1545-1554).

(*Id.* at Par. [0066]).

Ad5 gal was administered at the same time and from the same lot to control rats without cirrhosis. Rats with 5 and 8 weeks of CCl₄ intoxication and rats with 2 and 4 weeks of bile duct ligation (BDL) were sacrificed 72 hrs after administration of recombinant adenovirus for the histological analysis and determination of the expression of the galactosidase protein (gal) encoded by the AdR. For this purpose liver, spleen, heart, lungs, kidneys and brain were extracted, tissue sections were cut in cube shapes of 5 to 6 mm., which were absorbed in freeze medium Tissue-Tek O.C.T., the tissues were frozen at -30 °C. and they were cut with a cryostat to obtain 8 .mu.m sections These sections were placed on silanized glass slides and fixed with formaline, pH 8.5, during 15-30 minutes and were exposed to Xgal for 16-18 hours, being counterstained with Neutral Red stain. (Weiss D J. Ligitt D. and Clark J G. In situ Hiti Chemical Detection of galactosidase activity in lung: assessment of Xgal reagent in distinguishing 1AC-Z Gene expression and endogenous galactosidase activity. *Human Gene Therapy*, Sep. 1, 1997, 8:1545-1554). The percentage of positive cells was determined by morphometric analysis in multiple fields of the same size and calculating the average. Besides, liver sections of cirrhotic rats were obtained and tissues absorbed in paraffin were cut and stained with Sirius red which specifically stains collagenic proteins

(Armendariz-Borunda J., and Rojkind M., A simple quantitative method for collagen typing in tissue samples: Its application to Human liver with schistosomiasis. Collagen Rel. Res 1984, Vol. 4, 35-47). Through this technique we can verify clearly the degree of fibrosis and the increase of bile ducts in the hepatic parenchyma. To verify the in vivo transduction of cells with GFP, we used healthy Wistar rats that received pAdGFP MMP-8 vector. 72 hours later, a laparotomy was performed and the exposed organs were visualised in the microscope of fluorescence, closing the wound afterwards to keep the animal alive.

(*Id.* at Par. [0068]).

The preferred way to apply the present invention is through endovenous administration of the recombinant adenoviral vectors of this invention or the pharmaceutical compound which contains them, in which therapeutically effective amount is administered with an unitary dose regimen convenient to an individual with fibrosis. This regimen can be adjusted according to the affliction degree. Generally, unitary doses of about 10^7 to 10^{14} viral particles for individual are employed. The preparation of a pharmaceutical compound including the adenoviral recombinant vectors of this invention can be conducted through the employment of standard techniques very well known by the persons skilled in the art, in combination with any of the pharmaceutically acceptable carriers described in the state of the art, including without limitation, starch, glucose, lactose, saccharose, gel, malt, rice, wheat flour, chalk, silica-gel, magnesium stearate, sodium stearate, powder of glyceril monostearate, NaCl, glycerol, propylene glycol, water, ethanol, and similar. These compounds can take the pharmaceutical form of solutions, suspensions, pills, tablets, capsules, powders and slow release formula, and similar.

(*Id.* at Par. [0071]).

Applicants respectfully submit that the specification as-filed provided an enabling disclosure for the claimed compositions of the invention fulfilling the requirements of 35 U.S.C. § 112, first paragraph. Therefore, the rejection of claims 22 and 28-32 under 35 U.S.C. § 112, first paragraph, should be withdrawn.

With regard to method claims 24-27, Applicants also respectfully traverse the rejection.

In particular, the specification as-filed discloses:

AdRs containing LacZ and GFP (green fluorescent protein) reporter genes are capable of transducing livers of cirrhotic rats even if the lobular architecture of the liver is distorted.

(*Id.* at Par. [0063]).

Thus, we could send to these livers therapeutic genes such as human metalloproteases or collagenases human MMP-8 active and latent, MMP-1, MMP-2, MMP-9 and MMP-3; human Urokinase Plasminogen Activator (uPA wild type and/or modified); the truncated receptor for TGF- β type II and Smad 7, which degrade the excess of collagenic proteins deposited and/or prevent the exacerbated synthesis of collagenic proteins, as it is shown in FIGS. 2 and 18; and/or genes which encode for proteins stimulating hepatic regeneration such as uPA, in order to re-establish the normal functioning of the liver, as is shown in FIG. 2.

(*Id.* at Par. [0064]).

The current invention initiates a research line to carry out gene therapy as an alternative for the treatment of chronic degenerative disease, specifically of hepatic cirrhosis in human beings, through the establishment of an efficient vehicle to send genes to the liver which will produce therapeutic proteins to help re-establish the normal functions of the liver, see FIG. 2. FIG. 2 shows how sending efficiently a therapeutic gene to the liver, in this case, a collagenase (metalloproteases of matrix, MMPs), it is possible to promote degradation of collagen through the over-expression of these metalloproteases.

(*Id.* at Par. [0065]).

The models of experimental hepatic cirrhosis used are: a) Chronic intoxication caused by carbon tetrachloride (CCl₄), in which hepatic cirrhosis is established starting from the 8th week of peritoneal administration (Mion F, Geloën A, Agosto E. and Minaire Y. Carbon tetrachloride induced cirrhosis in rats: influence of the acute effects of the toxin on glucose metabolism. *Hepatology* 1996, Vol. 23, No. 2:582-587); and B). ligation of the bile duct (LCB) in which cirrhosis is observed after the fourth week of surgery (Lee S, Giraud C., Draillon A., HADengue A., and Lebec D., Hemodynamic characterization of chronic bile duct ligated rats; effect of pentobarbital sodium. *AM Journal fisiol.* 1986; 251:176-180; Nakano S., Harakane J. and Hashimoto H.,

Alteration in peribiliary ducts microcirculation in rats after common bile duct ligation. *Hepatology*, 1995, Vol. 21, No. 5: 1380-1995; Dumas Walla R., Belcowitz D., and H. Eubi J E. Adaptive response of the Enterohepatic circulation of bile acid to extra hepatic. *Cholestiasis Hepatology* 1996, Vol. 23, No. 3: 623-629 and Poo J. L., Stanes A., Pedraza-Chaverri J., Cruz C., Prez C., Huberman A. and Uribe M: Cronologia de la Hipertensin Portal, Disminucin de la Excrecin de sodio y activacin del sistema renina-angiotensina en cirrosis biliar experimental. *Rev., Invest Clin*, 49:15-23,1997).

(*Id.* at Par. [0067]).

Ad5 gal was administered at the same time and from the same lot to control rats without cirrhosis. Rats with 5 and 8 weeks of CCl₄ sub.4 intoxication and rats with 2 and 4 weeks of bile duct ligation (BDL) were sacrificed 72 hrs after administration of recombinant adenovirus for the histological analysis and determination of the expression of the galactosidase protein (gal) encoded by the AdR. For this purpose liver, spleen, heart, lungs, kidneys and brain were extracted, tissue sections were cut in cube shapes of 5 to 6 mm., which were absorbed in freeze medium Tissue-Tek O.C.T., the tissues were frozen at -30 °C. and they were cut with a cryostat to obtain 8 µm sections These sections were placed on silanized glass slides and fixed with formaline, pH 8.5, during 15-30 minutes and were exposed to Xgal for 16-18 hours, being counterstained with Neutral Red stain. (Weiss D J. Ligitt D. and Clark J G. In situ Hiti Chemical Detection of galactosidase activity in lung: assessment of Xgal reagent in distinguishing 1AC-Z Gene expression and endogenous galactosidase activity. *Human Gene Therapy*, Sep. 1, 1997, 8:1545-1554). The percentage of positive cells was determined by morphometric analysis in multiple fields of the same size and calculating the average. Besides, liver sections of cirrhotic rats were obtained and tissues absorbed in paraffin were cut and stained with Sirius red which specifically stains collagenic proteins (Armendariz-Borunda J., and Rojkind M., A simple quantitative method for collagen typing in tissue samples: Its application to Human liver with schistosomiasis. *Collagen Rel. Res* 1984, Vol. 4, 35-47). Through this technique we can verify clearly the degree of fibrosis and the increase of bile ducts in the hepatic parenchyma. To verify the in vivo transduction of cells with GFP, we used healthy Wistar rats that received pAdGFP MMP-8 vector. 72 hours

later, a laparotomy was performed and the exposed organs were visualised in the microscope of fluorescence, closing the wound afterwards to keep the animal alive.

(*Id.* at Par. [0068]).

The previous results that are presented here regarding the study of the physiopathology of experimental hepatic cirrhosis are summarized in FIG. 2. Said figure shows the role of pro-inflammatory and pro-fibrogenic cytokines produced *In vivo* by Kupffer cells which, in turn, activate the hepatic stellate cells (HSC) to have them produce excess collagens deposited in the subendothelial space, obstructing the exchange between hepatocytes and sinusoids (Armendariz-Borunda J., Katayama K., and Seyer J. M.: Transcriptional mechanisms of type I collagen gene expression are differentially regulated by IL-1beta, TNFalfa and TGF into cells. *J. Biol. Chem.* 267:14316-14321, 1992; Armendariz-Borunda J., Katai H., Jones C. M. Seyer J. M. Kang A. H. and Raghow R.: Transforming growth factor beta is transiently enhanced at a critical stage during liver regeneration following CCL4 treatment. *Laboratory Investigation.* 69:283294, 1993 and Armendariz-Borunda J., Roy N., Simjewish C., Raghow R. Seyer J. M. and Kang A. H.; activation of Ito cells involves regulation of API collagen Gene Expression. *Biochemical Journal* 304:817-824, 1994). The degree of incorporation of Lac-z gene in cultured cells showed visible differences between techniques of Calcium-Phosphate, DNA-polylisine-lactose complexes and with the recombinant adenoviral vector in HepG2 and PMM (Peritoneal mouse macrophages). The degree of transduction with adenovirus reaches 100% and with the other two techniques about 1% as shown in FIG. 5. FIG. 6 shows the expression of green fluorescent protein (GFP) in cultured cells. A). Peritoneal mouse Macrophage transduced with the adenoviral vector pAdGFP-MMP8, 72 hours after its administration (50 times), B).HepG2 cells transduced with the adenoviral vector pAdGFP-MMP8, 72 hours after its administration (50 times) and C). HepG2 cells without the adenoviral vector. All the pictures were taken In a microscope stereoscope of fluorescence. It is necessary to point out that in the development to identify galactosidase activity, the cells must be fixed and they die. In the GFP assay, the cells are still intact and alive.

(*Id.* at Par. [0069]).

FIG. 7 shows the expression of gal in different organs after infusion with Ad5 gal by iliac vein. Fixation, washing and Xgal solutions using different pHs were used to discriminate among the endogenous expression and the bacterial exogenous galactosidase. In figure A, a pH 7.0 was used and in Figure B the pH was 8.5. This is the summary of the results of the assays of the different experimental conditions and it can be appreciated that the tissue exposition to Xgal solution with a pH 8.5 allowed us to eliminate the expression of endogenous galactosidase. We obtained frozen tissue sections from different organs: liver, kidney, lung, heart, brain and spleen from normal rats and intoxicated with CCl₄ for five and eight weeks. As represented in FIG. 8, the graphics show clearly that the main target organ is the liver, both in healthy rats as well as in rats with chronic administration of CCl₄. A) 5 weeks of CCl₄ administration and B) 8 weeks of CCl₄ administration. Spleen and lung present a degree of transduction below 1%, and thus this is not evident from the graphs. Rats received doses of 3×10^{11} viral particles/ml of Ad5gal vector. The healthy control rats presented a total of 70% of hepatocytes transduced, while spleen and lung showed less than 1% transduction. In the other organs no transduction was found. Tissue sections were obtained from healthy rats as described before and compared with tissues from rats with 2 and 4 weeks of BDL. FIG. 9 clearly shows how the main target organ is the liver, both in healthy rats as well as in BDL rats. A) 2 weeks of LCB and B) 4 weeks of BDL. The spleen and the lung present a transduction grade lower than 1%, and thus it is hardly noticeable in graphs. With a dose of 3×10^{11} viral particles/ml of the Ad5gal vector, BDL rats present a total of 10% transduced hepatocytes. Besides liver, spleen and lung presented less than 1% transduction. The other organs showed no transduction. In FIG. 10, histological results are shown with the hepatic cirrhosis model induced by the chronic administration of CCl₄. A) represents a liver section of a normal rat, 72 hours after the administration of Ad5 gal, by iliac vein (one representative cut of the experiments of a total of 5 rats). More than 70% of the hepatocytes are positive to the expression of gal (200 times); D) The same liver as in Figure A, but stained with Sirius Red to observe collagen synthesis and deposition (200 times); B) liver with 5 weeks of chronic intoxication with CCl₄. About 30-40% of the hepatocytes were successfully transduced; E). The same livers as in B, but stained with Sirius Red, the increase in the amount of collagen is notable and the liver architecture begins to distort (200 times); C) rat liver after 8 weeks

of chronic intoxication with CCl₄ to cause cirrhosis, again more than 40% of liver cells were positive for β -Gal expression and F) the same livers as in C, but stained with Sirius Red. Large deposits of collagen formed between the central and portal veins (200 times) are characteristic. In FIG. 11, results obtained in the model of biliar duct ligation (BDL) induced cirrhosis are shown. A) shows a liver section of a normal rat 72 hours after the administration of Ad5 gal, by iliac vein (one representative cut of the experiments of a total of 5 rats). More than 70% of the hepatocytes are positive to the expression of gal (200 times); D) the same liver as in Figure A, but stained with Sirius Red to observe collagen (200 times); B) rat liver after 2 weeks of BDL. .beta.-gal essay was conducted 72 hours after Ad5 β -Gal administration, via iliac vein. About 10% of the hepatocytes were successfully transduced with the reporter gen; E) the same livers as in B, but stained with Sirius Red. Liver architecture begins to distort due to colestasis-induced fibrosis as well as to the important increase of biliar ducts (200 times); C) rat liver after 4 weeks of BDL to cause cirrhosis. .beta.-gal essay was conducted 72 hours after the administration of Ad5 β -Gal, via iliac vein. Again, 10% of hepatocytes were successfully transduced and F) the same livers as in C, but stained with Sirius Red. Observe the large deposit of collagen proteins formed as well as the proliferation of biliar ducts (200 times). FIG. 12 shows a laparotomy of a healthy Wistar rat that received pAdGFP-MMP-8 vector. The expression of the GFP is clearly seen in the liver and in insignificant amounts in the spleen. A very important fact is that the injection of adenoviral vectors did not induce lethal toxicity in experiment animals, both healthy and controls.

(*Id.* at Par. [0070]).

Applicants respectfully submit that the specification as-filed provided an enabling disclosure for the claimed methods of the invention fulfilling the requirements of 35 U.S.C. § 112, first paragraph. Therefore, the rejection of claims 24-27 under 35 U.S.C. § 112, first paragraph, should be withdrawn.

Applicants respectfully request that the rejection of claims 22-27 and 28-32 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

IV. The Rejections Under 35 U.S.C. § 102(b)

A. The Rejections

Claims 22 and 23 stand rejected on pages 6-7 of the office action under 35 U.S.C. § 102(b) as allegedly being anticipated by Hattori *et al.*, January 20, 1999 (Human Gene Therapy, Vol. 10, no. 2, pp. 215-222) (“Hattori”).

Claim 22 is rejected on page 7 of the office action under 35 U.S.C. § 102(b) as allegedly being anticipated by Jaffe *et al.*, April-May 1999 (Experimental Lung Research, Vol. 25, No. 3, pp. 199-215) (“Jaffe”).

Applicants are awaiting a certified copy of the priority document, Mexican Application Number 998515, as required by 35 U.S.C. § 119(b) and will submit the certified copy in a supplemental amendment as soon as it is received. Applicants respectfully submit that submission of the certified copy of Mexican application number 998515, filed September 17, 1999 will perfect the priority claim, and therefore the rejection of claims 22 and 23 under 35 U.S.C. § 102(b) as anticipated by Hattori and the rejection of claim 23 under 35 U.S.C. § 102(b) as anticipated by Jaffe will no longer be proper.¹

V. Conclusions

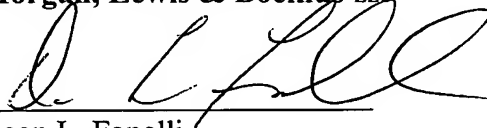
It is respectfully submitted that the rejections to the claims have been overcome. Should the Examiner disagree, Applicants respectfully request a telephonic or in-person interview with the undersigned attorney to discuss any remaining issues and to expedite the eventual allowance of the claims.

¹ Applicants note that the Examiner indicated that the claims could be rejected under 35 U.S.C. § 102(a). However, because the Examiner has not in fact rejected the claims under 35 U.S.C. § 102(a), the Applicants have not addressed the issue at this time.

Except for issues payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310.

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